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Bioactive Cyanoacrylate-based Filling Material for Bone Defects in Dental Applications

Kyeong-Jun Park[1,2,a], Ji-Ho Park[1,2,b], Sang-Bae Lee[1,c], Doug-Youn Lee[1,d], Kyoung-Nam Kim[1,2,e], and Kwang-Mahn Kim[1,2,f]

[1] Department & Research Institute of Dental Biomaterials and Bioengineering, Yonsei University College of Dentistry, Shinchon-dong, Seodaemun-gu, Seoul 120-752, South Korea

[2] BK21 Project for Medical Science, Yonsei University, 134 Shinchon-dong, Seodaemun-gu, Seoul 120-752, South Korea

[a] hanbyeot@hotmail.com, [b] parkjiho76@hotmail.com, [c] ridm@yumc.yonsei.ac.kr, [d] dlee1@mmm.com, [e] kimkn@yumc.yonsei.ac.kr, [f] kmkim@yumc.yonsei.ac.kr (corresponding author)

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Abstract. We tried to prepare a new filling material for bone defects using β-Tricalcium phosphate (β-TCP) particles and Histoacryl®. The aim of this study was to evaluate physical and bioactive properties of cyanoacrylate-based filling materials for bone defects in the dental field. The shear bond strength values of the Histoacryl® and β-TCP/ Histoacryl® compounds stored in double-distilled water decreased with the increase of the amount of added β-TCP. The temperature change of the β-TCP/ Histoacryl® compounds during polymerization decreased compared to that of the Histoacryl®. The cytotoxicity of the filling materials decreased when the amount of added β-TCP was increased. In the evaluation of bioactivity, hydroxyapatite (HA) was precipitated on the surface and inner space of the porous filling material 4 weeks after immersion in SBF. This precipitation of HA on the surface of the filling material was also confirmed in the XRD result. These results indicate that our novel β-TCP/Histoacryl® compounds have the potential to serve as filling materials for bone defects in the dental field.

Introduction

N-butyl-2-cyanoacrylate which is known as Histoacryl® has been widely used as a tissue adhesive. It is a liquid compound that polymerizes rapidly in the presence of hydroxyl ions. It has been reported that butyl and isobutyl cyanoacrylates are non-carcinogenic in living organisms unlike ethyl and methyl cyanoacrylate compounds [1]. However, Histoacryl® showed a little tissue toxicity when the adhesive was introduced deep into highly vascular areas [2]. Histoacryl® has a wide range of applications in surgery and has been reported to offer advantages, such as effective and immediate haemostasis, ease of application, bacteriostatic properties, and rapid adhesion to hard and soft tissue [3].

Using this Histoacryl®, we tried to prepare a new filling material for bone defects in the dental field. However, only Histoacryl® could not be used as a filling material because of its low bioactivity and formability, and a little toxicity. Among common bone cements, hydroxyapatite (HA) or tricalcium phosphate (TCP) is often incorporated as an additive in order to improve bioactivity for stimulating bone in-growth and mechanical fixation. Among both of them, TCP ceramics with a better resoption pattern can be gradually absorbed, followed by new bone formation and without loss of bone-implant contact. Especially, β-Tricalcium phosphate (β-TCP) shows that its structure and composition is similar to the inorganic part of the natural bone, and thus is often used to act as bone-grafting and dental materials [4]. Thus, we added β-TCP particles to Histoacryl® in order to improve bioactivity and reduce toxicity. The aim of this study was to evaluate physical and bioactive

properties of cyanoacrylate-based filling materials consisting of β-TCP and Histoacryl® for dental applications.

Materials and methods

A filling material was prepared by mixing Histoacryl® and acid-treated β-TCP particles. The acidic treatment of β-TCP was preformed by immersing β-TCP particles in a 1% citric acid solution at room temperature for 24 hours. Following the acidic treatment, the β-TCP particles were washed with double-distilled water and dried. Mixing weight ratios of acid-treated β-TCP to Histoacryl® were 4, 5, and 6, respectively.

The shear bond strength of the filling materials with bovine teeth was evaluated using a universal testing machine (Instron, Cambridge, UK). The surfaces of each tooth were polished with No. 100 and No. 600 silicon carbide papers. The specimens for shear bond strength were prepared by bonding between one tooth mounted in a resin holder and the other with an area of approximately 5 mm × 5mm using the filling materials. The prepared specimen assemblies were then stored in air and in double-distilled water at 37℃ for a period of 7 days. Testing was carried out at a crosshead speed of 1 mm/min with a shearing blade. The shear bond strength was estimated as load at failure per specimen surface area.

The temperature change of the filling materials during polymerization was measured using a thermal couple recorder (Yokogawa Electric Corporation, Tokyo, Japan). The filling material and a small quantity of double-distilled water were mixed in the mold and simultaneously, the temperature change during polymerization was measured until the final temperature became constant.

The cytotoxicity of the filling materials was evaluated by an agar diffusion test. The established L929 cells, with a concentration of about 1×10^5 cells/ml, were used. The agar media were allowed to gel at room temperature for 30 min. Each agar medium was then stained with a neutral red vital stain solution for 1 hour. A couple of rectangular specimens of the filling materials, with an area of 5 mm × 5 mm, were overlaid onto each petri-dish filled with the agar medium with a negative (polyethylene) and positive (polyvinylchloride) control after removing the stain solution. Each petri-dish was subsequently incubated under a humidified 5% CO_2 air atmosphere at 37℃ for 24 hours. The decolorization and lysis indices were determined under a light microscope (Olympus, Tokyo, Japan). Decoloration index was detected by the grade of the decolorizing cell zone and the lysis index was measured by the grade of cell lysis under the place that is the specimen location.

In order to evaluate the bioactivity of the filling material with the β-TCP/ Histoacryl® ratio of 5, the specimens with a dimension of $10 \times 10 \times 1$ mm^3 were immersed in 20 ml of an acellular SBF with ion concentrations similar to that of human blood plasma at 37℃ for 4 weeks, respectively. The SBF was prepared by dissolving reagent grade NaCl, $NaHCO_3$, KCl, $K_2HPO_4\bullet3H_2O$, $MgCl_2\bullet6H_2O$, $CaCl_2$, and Na_2SO_4 in double-distilled water and buffering at pH 7.4 at 37□ with tris-hydroxymethylaminomethane [$(CH_2OH)_3CNH_2$] and 1M hydrochloric acid (HCl). The SBF was renewed every other day. After immersion in the SBF for 4 weeks, the surfaces of filling materials were washed gently with double-distilled water and dried for 24 hours. The surface morphology of the immersed filling materials was observed using a scanning electron microscope (SEM; Hitachi, Tokyo, Japan). The crystallinity and structure of the surfaces of the immersed filling materials were examined using an X-ray diffractometer (XRD; Rigaku, Tokyo, Japan).

Results

The filling material with β-TCP/ Histoacryl® ratio of 6 hardly maintained its shape unlike the filling materials with β-TCP/ Histoacryl® ratios of 4 and 5 after hardening. Thus, the formability of the filling materials got worse with the increase of the amount of added β-TCP.

Fig.1 shows the shear bond strength 7 days after the filling materials were stored in air and in double-distilled water, respectively. The shear bond strength values of the Histoacryl® and β-TCP/ Histoacryl® compounds stored in air were not significantly different. However, the shear bond strength values of the Histoacryl® and β-TCP/ Histoacryl® compounds stored in double-distilled water decreased with the increase of the amount of added β-TCP. Especially, the shear bond strength values of the β-TCP/ Histoacryl® compounds stored in double-distilled water were much lower than that of the Histoacryl®, unlike those stored in air.

Fig.2 shows the temperature change when the filling materials were polymerized. The temperature changes of β-TCP/ Histoacryl® compounds during polymerization were much lower than that of Histoacryl®. However, the temperature changes of the β-TCP/ Histoacryl® compounds during polymerization were not significantly different irrespective of the β-TCP/ Histoacryl® ratios.

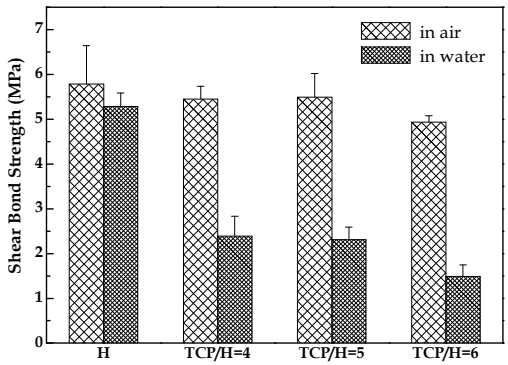

Fig. 1. Shear bond strength

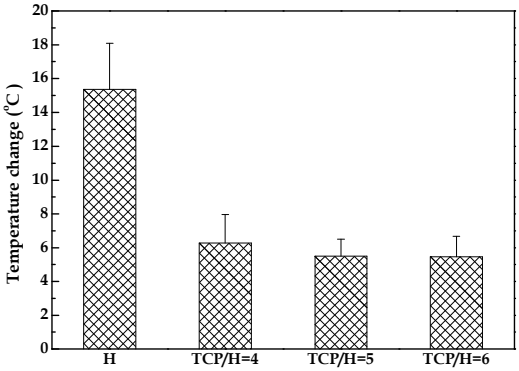

Fig. 2. Polymerization temperature change

Table 1 shows the cytotoxicity of the filling materials as well as controls determined by an agar diffusion test. Histoacryl® showed moderate cytotoxicity. However, the cytotoxicity of the filling materials decreased with the increase of the amount of added β-TCP.

Table 1
Cytotoxicity of the filling materials as well as controls determined by agar diffusion test

Specimens	Response index (Zone index / Lysis index)	Cytotoxicity
Histoacryl®	3 / 3	Moderate
β-TCP/ Histoacryl® = 4	2 / 5	Moderate
β-TCP/ Histoacryl® = 5	2 / 1	Mild
β-TCP/ Histoacryl® = 6	1 / 1	Mild
PVC (positive control)	4 / 5	Severe
PE (negative control)	0 / 0	None

Fig.3 shows the surface morphology of the filling material with the β-TCP/ Histoacryl® ratio of 5 before immersion and 4 weeks after immersion in SBF. The surface of the prepared β-TCP/ Histoacryl® compound showed porous structure consisting of β-TCP particles covered with Histoacryl®. HA was precipitated on the surface and inner space of the porous β-TCP/ Histoacryl® compound 4 weeks after immersion in SBF. The precipitated HA consisted of sphere-shaped crystallites with a size of about 0.2 μm.

Fig. 4 shows the XRD patterns of the filling material with the β-TCP/ Histoacryl® ratio of 5 before, 2 weeks, and 4 weeks after immersion in SBF. As immersion time in SBF increased, a new peak indicating HA appeared and the intensity of the peak also increased. In addition, the intensity of peaks representing β-TCP decreased with the increase of immersion time in SBF.

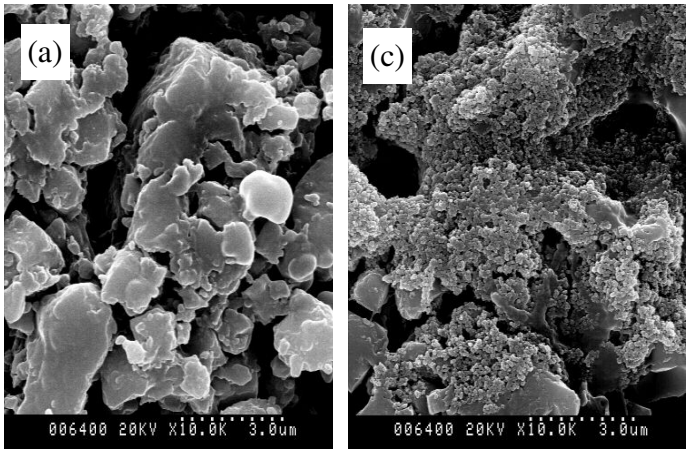

Fig. 3. Surface morphology

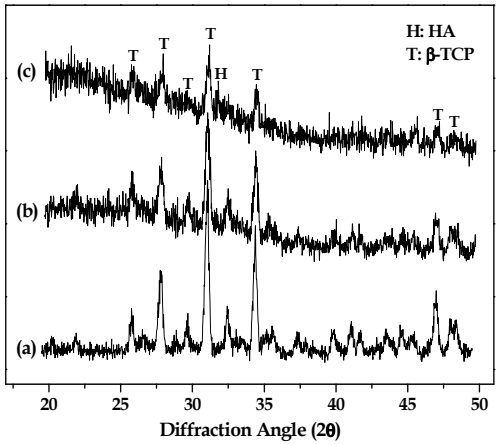

Fig. 4. XRD patterns

(a) before, (b) 2weeks, and (c) 4 weeks after immersion in SBF

Discussion and conclusion

The present study demonstrated that the β-TCP/ Histoacryl® compound, with the proper amount of β-TCP, could be used as a filling material for bone defects. First, the filling materials showed low formability with the increase of the amount of added β-TCP. This indicates that the mixing weight ratio for β-TCP/ Histoacryl® compound should be controlled properly. The shear bond strength of the filling materials stored in double-distilled water for 7 days decreased with addition of β-TCP. Although the shear bond strength of β-TCP/ Histoacryl® compound got lower compared to that of the Histoacryl®, it is considered that it can be sufficient enough to maintain bonding with bone for a long period of time. In addition, the temperature of the β-TCP/ Histoacryl® compound during polymerization did not increase highly compared to that of the Histoacryl®. This indicates that the added β-TCP interfered heat generation of the Histoacryl® during polymerization. The addition of β-TCP also decreased the cytotoxicity of Histoacryl®, preventing toxic chemicals from being released into surrounding tissues. Finally, the bioactivity of the filling materials was demonstrated with SEM and XRD results 4 weeks after immersion in SBF. This bioactivity means that the bonding between the growing bone and the filling materials can be accelerated and fixed more tightly at the same time with the degradation of filling materials in the human body. Moreover, it is expected that the filling material may be fixed in bone defect more quickly and firmly due to the adhesive ability of Histoacryl® to hard tissue. Therefore, this bioactive cyanoacrylate-based material, consisting of β-TCP and Histoacryl®, has good potential for the filling of bone defects in dental applications.

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References

[1] S.N. Bhaskar *et al.*: J. Am. Dent. Assoc., Vol 77 (1968), p. 831
[2] J. Quinn *et al.*: Clin. J. Sports Med., Vol 4 (1994), p. 245
[3] G.B. Giray *et al.*: Aust. Dent. J., Vol 42 (1997), p. 255
[4] S.M. Kuo *et al.*: J. Appl. Polym. Sci., Vol 89 (2003), p.3897